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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/937,070	01/29/2002	Thomas C. Evans	NEB-177-PUS	4532

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EXAMINER	
SCHNIZER, HOLLY G	

ART UNIT	PAPER NUMBER
1656	

DATE MAILED: 09/21/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/937,070	EVANS ET AL.	
	Examiner	Art Unit	
	Holly Schnizer	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 July 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1-10,12,19 and 20* is/are allowed.

6)☒ Claim(s) *11 and 13-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *20 November 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

The Amendment and Response filed July 5, 2006 has been entered and considered. Claims 1-20 are pending and have been considered in this Office Action.

Rejections Withdrawn

The rejection of Claims 1, 3-11, and 14-18 under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps is withdrawn in light of Applicants arguments. See MPEP § 2172.01. The claimed methods are incomplete because they do not have a method of eluting the polypeptides from the column. Incorporation of the limitation of Claim 2 into Claim 1 and Claim 13 into Claim 11 would overcome this rejection.

The rejection of Claim 13 under 35 U.S.C. 112, 2nd paragraph for reciting the limitation "said solid support" in line 2 without antecedent basis is withdrawn in light of the amendment.

Rejections Maintained

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 11, 13-18 are rejected under 35 U.S.C. 102(a) as being anticipated by Evans et al. (J. Biol. Chem. (June 25, 1999) 274(26): 18359-18363; ref. BG of IDS filed 10/15/01).

Restatement of Rejection

Evans et al. teaches a method of making a cyclic polypeptide by fusing the C-terminal portion of a split intein (Ssp mini-intein) to the N-terminus of a target polypeptide (BBP, RGD, or CDR-H3/C2) and fusing the N-terminal portion of a split intein (Mxe GyrA intein) to the C-terminus of the target to produce a fused polypeptide, fusing an affinity binding domain (a chitin binding domain) to the fused polypeptide, immobilizing the fused product on an affinity based solid support (chitin column), incubating the immobilized precursor under conditions that favor formation of the cyclic polypeptide, and eluting the cyclic polypeptide from the solid support (see p. 18360). BBP, RGD, and CDR-H3/C2 are cyclic peptides. The inteins used in the method of Evans et al. appear to be artificially split inteins. An artificially split intein and a naturally split intein have identical function and could not be distinguished from each other except by knowing how they were made. Thus, Claim 16 is rejected because an artificially split intein is not patentably distinguishable from a naturally split intein. Thus, Evans et al. meets the limitations of the claims.

Response to Applicants' Arguments

Applicants argue that Evans et al. is authored by the applicants and is not an invention by others. This argument has been considered but is not deemed persuasive because the term "others" in 35 U.S.C. 102(a) refers to any entity which is different from

the inventive entity or, in other words, any combination of authors or inventors different than the Inventive Entity (see MPEP 2132(III)). The inventors of the present application are Evans and Xu. The authors of Evans et al. include Evans, Benner, and Xu. Thus, Evans et al. is considered "by others".

Applicants argue that Evans et al. uses intact inteins and not split inteins as required by the present claims. Applicants compare Figure 1 of Evans with Figure 3 in the present Application to support their position. This argument has been considered but is not deemed persuasive for the following reasons. What is to be compared in determining prior art is whether the reference teaches what is claimed and not necessarily what is in the drawings. The present claims are not patentably distinguishable from Evans et al. including Figure 1 of Evans et al. Split inteins are intein fragments that come from two genes—one with the N-terminal intein function and one with the C-terminal intein function. The two inteins used in Evans et al. are Ssp mini intein and Mxe GyrA intein. Both of these inteins have been modified to have either N-terminal activity (Ssp mini-intein) and C-terminal activity (Mxe GyrA) and thus are not considered patentably distinguishable from split inteins. If Evans et al. differs because the two intein fragments used in therein are not complementary then this needs to be added as a limitation to the claim to distinguish it from Evans et al. Otherwise, absent evidence of a difference between the presently claimed invention and the method of Evans et al., it appears that they are patentably indistinguishable.

New Rejection

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 11 and 13-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Evans et al. (J. Biol. Chem. (June 25, 1999) 274(26): 18359-18363; ref. BG of IDS filed 10/15/01) in view of Wu et al. (Proc. Natl. Acad. Sci. (Aug. 1998) Vol. 95, pp. 9226-9231; ref. CF of IDS filed 10/12/01).

Evans et al. teaches a method of making a cyclic polypeptide by fusing the C-terminal portion of a split intein (Ssp mini-intein) to the N-terminus of a target polypeptide (BBP, RGD, or CDR-H3/C2) and fusing the N-terminal portion of a split intein (Mxe GyrA intein) to the C-terminus of the target to produce a fused polypeptide,

fusing an affinity binding domain (a chitin binding domain) to the fused polypeptide, immobilizing the fused product on an affinity based solid support (chitin column), incubating the immobilized precursor under conditions that favor formation of the cyclic polypeptide, and eluting the cyclic polypeptide from the solid support (see p. 18360). BBP, RGD, and CDR-H3/C2 are cyclic peptides. The inteins used in the method of Evans et al. appear to be artificially split inteins. However, even in the case that the inteins used in the method of Evans et al. are distinguishable from split inteins, the teachings of Evans et al. combined with the teaching of split inteins would render the present claims obvious.

Wu et al. provides evidence that both naturally occurring and engineered split inteins were known in the art at the time of the invention. Wu et al. discloses the characterization of the naturally occurring split intein, Ssp DnaE and indicates that split inteins had already been engineered in vitro (p. 9230, Col. 2, last lines of first paragraph).

Thus, it would have been obvious to one of ordinary skill in the art to modify the method of Evans et al. to use either a split intein or naturally occurring intein in place of the inteins used therein. One of ordinary skill would have been motivated to do so since split inteins are smaller and can be engineered to have the desired activities.

Conclusions

Claims 11 and 13-18 are rejected. Claims 1-10, 12, and 19-20 appear to be free of the prior art of record.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Holly Schnizer whose telephone number is (571) 272-0958. The examiner can normally be reached on Tuesday, Thursday, and Friday from 10 am to 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr can be reached on (571) 272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

September 15, 2006

HOLLY G. SCHNIZER, PH.D.
PATENT EXAMINER